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## SECTION OF THE HISTORY OF MEDICINE.

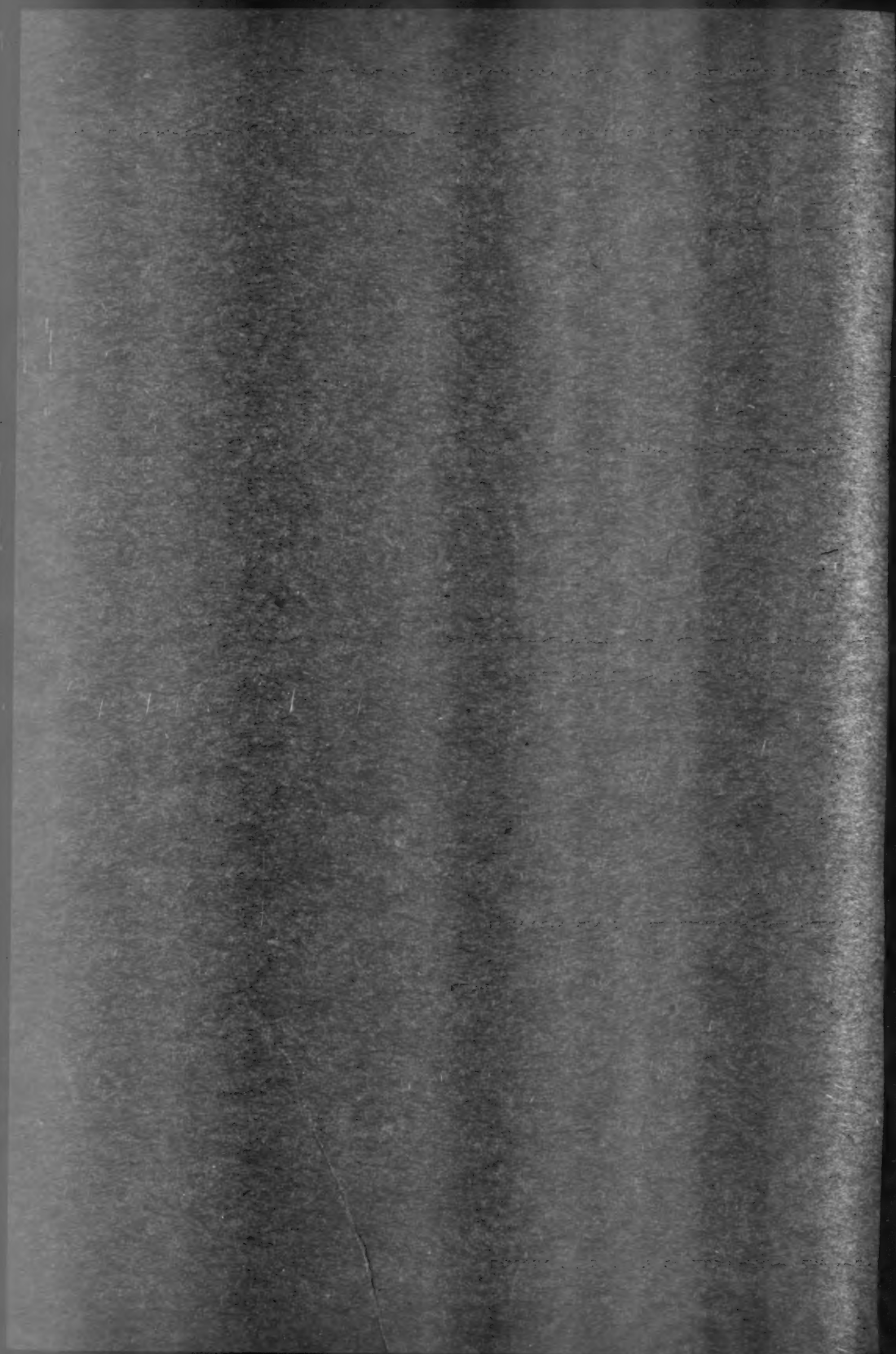
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## Section of the History of Medicine.

President—Sir D'ARCY POWER, K.B.E., F.R.C.S.

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### A Note on the History of Epidemic Encephalomyelitis.

By F. G. CROOKSHANK, M.D.

"On l'a dit justement, les mêmes questions renaissent à chaque épidémie catarrhale, et leurs solutions diverses se reproduisent chaque fois à peu près les mêmes."

BOUVIER (*Ann. d'Hygiène Pub. et de Méd. Légale*, 1837).

THE clinical manifestations which of late years have become associated with the names of encephalitis acuta hæmorrhagica, polio-encephalitis, poliomyelitis and so forth, have, there is little doubt, prevailed from time to time, during many centuries, in epidemic form.

The occurrences are not new; they have been described again and again in unmistakable language: but, since the overlying nosological, pathological, and ætiological conceptions have been ever-varying, we have failed to recognize the historical continuity of the realities. The history of epidemic encephalomyelitis is, therefore, not that of "one disease," but of many; for what we call "diseases" are not natural objects, but conceptual.

We may indeed apply to encephalomyelitis in some degree the words employed by Michel Lévy, in the *Gazette Médicale de Paris*, or 1849, concerning cerebro-spinal meningitis:—

"... point une nouveauté: confondue avec les fièvres cérébrales ataxiques, nerveuses: perdue dans les énumérations banales et dans les généralités graphiques des épidémistes et des chroniqueurs de la médecine: mêlée à d'autres épidémies plus considérables, comme le typhus, et rattachée à ses manifestations, à titre d'anomalie ou de

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variété anatomique . . . elle échappe à une détermination historique rigoureuse à cause de l'insuffisance ou de l'ambiguïté des documents, de l'absence ou de l'imperfection de l'anatomie pathologique."

Nevertheless, though, like Lévy, we may not wish "nous exposer à juger aujourd'hui sous l'optique d'une préoccupation synthétique," we must, as did he when observing the almost concurrent outbreaks of cerebro-spinal meningitis and influenza at the Val-de-Grâce, declare that "lorsqu'on voit . . . des combinaisons morbides qui déroutent l'observation vulgaire, l'idée de la continuité des épidémies se présente derrière le fait incontestable de leurs connexions."

This however is true: since the prevalences of encephalomyelitis have been irregular and intermittent, and the clinical pictures "protean," almost every epidemic has been hailed as a new disease by many, and described in new terms by someone. Nevertheless it is surprising that only one author, Ozanam, appears to have attempted the history of epidemic encephalitis, and that his work should have been ignored by those who have written the history of poliomyelitis, or the Heine-Medin disease, as well as by medical historians in general. The fact is that those who have written the history of diseases have persistently confused names, notions and realities.

Julien Le Paulmier, writing at Paris, in 1578, "de morbis contagiosis," observed that the epidemic pestilences due to heavenly influences, are, some grave, and some mitigated, while some are familiar and others unusual, or unaccustomed. And he gave three instances of unaccustomed pestilences, appearing suddenly, as if new diseases.

The first, said Le Paulmier, is the sydropyreton (or sudor Anglicus of 1529) "quæ nostro hoc seculo Britanniam mire afflixit": the second, "destillatio quædam popularis nostris vernaculi *Coqueluche* appellata quæ in nostram hanc Galliam anno 1551 primum suevire cooperta sit" (in other words, the influenza which afflicted France during the time of the fifth and last "sweat" in England); and the third, "paraplegia inaudita sed lethalis quæ in Thaso contigit, flagrantes ardores gravedines anhelosæ aliique non pauci veterum oblivione deleti."

Of the two first, presently.

But what was this paraplegia in Thasus?

Hippocrates, in writing on epidemical diseases, says that in Thasus—  
I quote from Clifton's translation:—

"During this state of the weather, in the winter, Paraplegias began and attacked many, some of whom dy'd in a short time, for the disease

was very epidemical. In other respects they were well. But, in the very beginning of the Spring, Burning Fevers came on, and continued to the Equinox, and even to the Summer. Most of those escaped who were seiz'd presently after the beginning of the Spring and Summer, and some few dy'd: but when the Autumn and wet weather set in, they prov'd mortal to many. These fevers were of such a nature that where any one bled freely and plentifully at the nose he was sav'd by it more than by anything else."

The Hippocratic constitution for this year was, it is obvious, almost identical with that of 1918; epidemic paraplegia taking the place of our epidemic encephalitis "lethargica." The observation of Hippocrates was doubtless just: for the prevalences of encephalomyelitis have invariably stood in a certain relation to epidemics, and endemic-epidemics, of the "burning-fevers" that we call influenza.

I do not, however, wish to occupy your time with citations from the ancients: it is more convenient to begin with the century of da Vinci and Buonarrotti—in what doctors think the dark ages, when, however, as Hallam suggests, "some parts of physical science had already attained a height which mere books do not record."

\* \* \* \* \*

In the last 450 years four periods seem to be indicated in respect of epidemic encephalomyelitis: four periods marked by different phases of medical thought and observation.

During the first, which closes with the era of Willis and Sydenham, wide epidemic prevalences were observed and compared, as a rule, without resolution into component "diseases"; and symptoms, obviously due to forms of meningitis, encephalitis, and myelitis were described in relation to vast occurrences that we would now call "disease-groups."

In the second period, which roughly coincides with the eighteenth century, systems of nosology were based upon symptoms; and symptom-groups due to encephalitis and myelitis, as well as to meningitis, were referred to nervous, comatose, lethargic, stuporose, convulsive, apoplectic, and paralytic fevers, usually considered as different elements of special epidemic constitutions.

During the third period, which commenced about the year 1800, persistent efforts were made to distinguish specific diseases by the findings of morbid anatomy. Cerebritis, encephalitis, meningitis, and myelitis were then described, sometimes as "specific entities," sometimes as characteristic lesions of specific fevers such as "cerebral



typhus" and the like; sometimes again as evidences of metastasis of disease from one part of the body to another.

The fourth period, which commenced some thirty years or more ago, is characterized by the distinction of many specific diseases by association with specific organisms. It is to be hoped that this period will prove one in which medicine will so far profit by biology as not to neglect synthetic research in the pursuit of purely analytical investigation.

There is, however, throughout the whole history of these 450 years one tendency in continuity that is manifested by the persistent ascription of certain odd, detached prevalences of encephalomyelitis to varieties of food poisoning.

The Germans in 1529 ascribed some of the maleficent forms of the sudor Anglicus to the eating of fish; and, in 1820, Justin Kerner, of Weinsberg, attributed outbreaks, clinically identical with polio-encephalitis, to the eating of Swabian sausages; thereby laying the foundation of the myth of botulism. But it has long been also the custom in Germany to incriminate ergot of rye as the cause of certain acute, epidemic, and generally febrile maladies, characterized by respiratory and gastro-intestinal catarrhs, and exhibiting, as their cardinal symptoms, delirium or stupor, paralysis or convulsions and tremors, and interference with the special senses. These maladies frequently entailed permanent paralysis and withering of limbs, since they affected the young at least as frequently as (according to some authorities more frequently than) their elders.

This was the affection or group of affections known popularly in Germany (*inter alia*) as Kriebelkrankheit: called Raphania in Sweden by Linnæus, since he thought it due to radish-seeds and not to ergot; and, during the last fifty years replaced in the minds and text-books of Swedish physicians by cerebro-spinal meningitis, poliomyelitis and polio-encephalitis.

The unravelling of its tangled history is no easy task, yet lightened by detection of the mystification and suppression of facts practised by some of the German writers whose works have attained renown at the expense of far greater French and Italian epidemiographers. It is in great part this belief in the existence of an *acute*, epidemic, protean, febrile, paralytic, and spasmodic, non-gangrenous form of ergotism that has so long confused the history of encephalo-myelitis: and the mystery of its alleged restriction to Germany, Scandinavia and Russia entirely disappears when we find the same malady described



in England, in France, in Spain and in Italy, under different names. For, it was not the disease so much as the ætiological conception that had a restricted area of distribution.

It is worth recalling, too, that Reusner of Frankfort, when writing of the scurvy in 1600, spoke of the Kriebelkrankheit as characterized, when it appeared in 1595, by "veternus, mania, lumbago, paralysis, convulsiones et morbus Herculeus," and declared that: "ob symptomatum insolentiam novum esse suspicatum fuit."

To revert however to the first of Julien Le Paulmier's unfamiliar pestilences, I will only remind you that, while we know very little of the clinical features of the English sweats (save that stupor was a prominent feature of the grave cases) Dr. Hamer has clearly shown the epidemiological features to be those of influenza. The myth that the sweats were, save for that of 1528-29, confined to Englishmen, may be considered now exploded, for each sweat in England corresponded very closely in time to an epidemic, in every European country, that can be demonstrated to have been either influenzal, or encephalitic, or both. It was the *name* that had so restricted an application; the nature of the coqueluche or trousse-galant in France, the Hauptkrankheit in Germany, and the mal mazzuco in Italy cannot be seriously disputed. Nor is it difficult to place the strange disease that, according to Jean de Troyes and de Mézeray, spread through France in 1481-82.

This epidemic, "qui attaquoit aussi bien les grands que les petits," "qui mettoit le feu à la teste,"—this "maladie de fièvre et rage de teste," if Zeviani's interpretation of an allusion by Alessandro Benedetto is well founded, was contemporaneous, not only with the epidemic encephalitis (Hecker) or Hauptkrankheit that afflicted Germany and is mentioned in the Frankfort Chronicles, but with a catarrhal and pleuritic epidemic in Italy. It was soon followed by the first "sweat" in England.

I do not propose now to deal at length with the English "sweats." It must suffice to say that a fresh examination of many early continental authors makes it abundantly clear that Dr. Hamer's contentions are just.

It is beyond reasonable doubt that the absurd legends which represent the "sweats" as a disease "sui generis" and, save in 1528-29, afflicting Englishmen only, would not have attained their present currency had the laborious but wrong-headed erudition of Gruner, Hecker, Haeser, and Hirsch been called in question by some

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one conversant with practical and historical epidemiology before Dr. Hamer delivered his Milroy Lectures (1906). The "sweats" were "influenzas" of malignant and nervous type in some years and places, but often ephemeral, and of the nature of the summer epidemic in 1918.

Since however the sweat of 1529 was so copiously described in Germany, it is worth recalling that, according to Schiller and others who gave contemporary accounts, the disease was of an extremely variable character, assuming different guises in different places; and of all grades of malignancy. It commenced with short shivers, and, in malignant cases, with convulsions; whilst dizziness and tinnitus were common. Formications, cramps, and weariness, muscular weaknesses, affections of the nerves, of the brain, pain in the head and stupor ("somnolentia inevitabilisque sopor") were amongst the symptoms in some places of a malady which struck all classes of society and carried off some victims in even a few hours. The breathing was "as if the lungs were seized with incipient paralysis," whilst later "the spinal marrow was affected."

"Contra, quibus sudor non satis fluxit aut repulsus fuit, mortui sunt, vel asphyxia vel tabe et decidentia membrorum vel paralyti et obnigatione manuum atque pedum."

In those who escaped with their life, paralytic consequences of various kinds were noted.

The very clear indications, in Schiller's tract, that epidemic encephalomyelitis prevailed in Germany during the "English sweat" of 1529 in that country, have by most authors been either slurred over or treated as evidence of "ergotism," much in the same way as some Patagonian historian, in years to come, may write of the prevalence of "botulism" in England during the "Spanish" influenza of 1918.

And it is interesting to note that, although Gruner, Hecker, Haeser, and Hirsch all declared France to have been spared the "sweat" in 1529, there is nevertheless the clearest evidence, in Paradin's "*Histoire de Nostre Temps*," of a malignant and neurotoxic influenza—"une nouvelle maladie et inconnue aux médecins"—which ravaged France in that year.

"A cette nouvelle maladie fut nouveau nom imposé, et fut nommé *Trousse galand* pour la contagieuse mort qui s'en ensuivoit, avec grande et impourvue soudeinneté."

"Stop-gallant," be it noted, was the name given to our later "sweats" in England.

It is perhaps true that it was only during times of epidemic, and not always then, that the relation of the "nervous" cases and case-groups to the sudoral and catarrhal cases and cases-groups was recognized; but Benedetto, when writing "*de destillatibus sive catarrhis*" (*Omnium a vertice ad calcem morborum signa*), showed that he, at any rate, connected the signs and consequences of what we now call polio-encephalitis and poliomyelitis with the oftentimes epidemic catarrh. Fernel, moreover, who had written of new diseases in much the same strain as Le Paulmier (*De abdit. rerum causis*: lib. ii, cap. xi) had come to much the same conclusion.

I can only mention in passing, and without comment, the stuporose epidemic in Piedmont and Savoy during 1545-46, described by Sanders and by Ambroise Paré. It too, like the 1529 affair, was called Trousse-galant, and it was moreover contemporaneous with a "Haupt-weh" in Germany (1543-44-45-46) and a camp-disease at Boulogne.

"Trailers," in Leichtenstern's terminology, straggled on during the fifties, and even later, whilst the great pandemic influenza of 1580 had an *avant-coureur* in 1576, described by Ballonius, the French Sydenham. In Yvaren's translation we read thus: "Durant tout l'hiver et au commencement du printemps, il y eut une quantité innombrable de paralyses, et elles ne dépendaient pas seulement d'une fluxion froide partie de la tête . . . on rapportait celle-ci à l'état du ciel."

And Ballonius observes: "Les affections catarrhales se portent-elles à l'extérieur, ou de la tête au organes sous-jacents, on voit naitre des paraplégies et des hémiplegies."

The great influenza of 1580 was, in some places, so sudoral that many declared it the English sweat come back again, and so cephalic that Brunner called it too the Hauptkrankheit. Sennert himself said of it:—

"Nonnullis infestavit perpetua in somnia propensio ut in peste fieri solet."

By pestis he meant, of course, the Pestis Britannica of 1529. The next year, 1581, however was marked at Lüneburg, in North Germany, by an epidemic of palsies in the head and limbs (described by Ronsseus) that, like an outbreak in Belgium during the "influenzas" of 1557-58, has found a place in the later chronologies of "convulsive ergotism." Of this notable epidemic an admirable account is given

by Schenkus, copied almost verbatim from Ronsseus, in which are used the very adjectives "novus," and "inauditus," employed by Reusner for the same disease when it reappeared fifteen years later. Schenkus said that it was difficult to determine whether the malady was epidemic or endemic: and made no suggestion whatsoever of ergotism. The illness began with spasticity and palsy of the hands and feet: the patients, sometimes delirious, were often slumberous. The half closed eyes and open mouth filled with ropy mucus, and the tongue, affected as if paralysed, all remind us of the descriptions of the botulists: but the statement that sometimes those who recovered found the hands and feet to have lost their office as if the limbs were luxated, makes it clear that flaccid palsies were no unusual sequelæ.

Comparison of this account with one of the "spasmodic" form of Heine-Medin disease described in Australia by Breinl in 1917, forms one of the most instructive parallels in medicine. The coincidence extends even to the occurrence, in both groups of cases, of severe gastro-intestinal disturbances, as in some of ours during 1918.

In the last decade of the sixteenth century scattered prevalences now recognized as influenzal were freely interspersed by great trailing epidemics very similar to this at Lüneburg, but generally known popularly as Kriebelkrankheit, or Krampfsucht. It is clear from the accounts of both Sennert and Horst that no symptom nor sign of poli-encephalitis, poliomyelitis, or cerebro-spinal meningitis was lacking; and Sennert is emphatic that while "nunc cum febre, nunc sine febre," "neque contagio hoc malum carebat."

Neither Horst nor Sennert paid attention to the vulgar ætiology of ergot, chick-peas, bad bread, sour apples, mushrooms and the like. They regarded the malady as a "malignant fever with spasms." And, in 1772, Schleger, in a delightful but rhetorical essay, exposed clearly the repeated statement of Baldinger and others that this epidemic had been shown to be ergotic by those who, at the time, described it.

Now, in 1597, whilst this malady was raging, or trailing in Germany, the mal mazzuco appeared in Italy as it had already in 1529—the year of the sudor Anglicus. Zeviani, in 1804, brought forward evidence in favour of the view that this mal mazzuco was an intensely "nervous" form of influenza, and showed clearly that stupor, and katatonia (malum attonitum), were prominent amongst its symptoms.

To reinforce the point, that "epidemic catarrh" was widespread in 1597, he cited Schenkus who, writing contemporaneously, appears

to identify the Italian epidemic of 1597 with one which invaded Germany "ipso tempore." Zeviani, whose monograph on the epidemic catarrh is one of the best accounts of influenza ever written, identified realities, and refused to be a slave to names and notions.\*

A few more words are necessary on this question of the mal mazzuco. Zeviani cites, from Brassavola (Index in Galen), a passage which, though doubtless authentic, I have failed to find in those prodigious folios. It runs thus: "Pulsus affectus ex phrenitide et lethargo quem nos vocamus malum Mazuchi." Pretty clearly then, this mal mazzuco was a "clinical entity." It occurred in Sicily, and elsewhere, about 1504-5, at the same time as "encephalitis" in Germany, and shortly before our second "sweat" in England. It was notoriously present in Italy during 1529, when, according to the Teutonic epidemiographers, that peninsula escaped the "sweat," and it recurred at intervals until 1597.

Zeviani was right: the mal mazzuco was an epidemic nervous "disease," closely allied to influenza, of which he considered it a form, or derivative. The clinical picture was variable: occasionally "meningeal," sometimes convulsions, and at others stupor, lethargy, and catalepsy were characteristic symptoms.

It was compared vulgarly, at times, to the cysticercus disease of the sheep, and hence became known as "morbus ovinus," and "morbus arietis." The contemporary name in Germany for influenza was "Schaffkrankheit"; an appellation which, by a happy confusion, was in 1712 given by Camerarius as "Schlafkrankheit."

There is, after 1600, a long, almost silent, period in the history both of influenza and of all forms of encephalomyelitis. But the famous prevalences of 1657-58, described in England by Willis, and marked in the autumn of the latter year by a strange fever "whereby men were grievously affected in their brains and nervous stocks," was signalized at Copenhagen, in 1657, by an epidemic of lethargy, or lethargic encephalitis, that makes the constitution for that year of an even juster parallel with that of 1918 than was that of Hippocrates already mentioned.

I do not think Bartholin's account has been referred to for a hundred years, and therefore cite it, almost in full:—

"Hyems frigida quidem, sed sine multa nive, in urbe nostra affectus soporosos excitavit, accuratis periodis molestos. Non pauci nostra cura soporem perpetuum evasere. A meridie sopor mensis spacio obrepabat, et ab astantibus excitati in somnum relabebantur. Expurgato capite

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et exsiccatō, imprimis cucurbitulis dorso affixis convaluerunt. Vere ejusdem anni Pleuritides Epidemiæ grassabantur, cum febre acuta doloribus pungivitis. . . . Declinante verò æstate, febres ephemeræ invaluerunt, spacio 24 horarum desinentes, invadentesque cum vomitu, calore intenso perdurante. . . .

"Ecstasi quadem correpti de capitis, doloribus conquerebantur. Nonnullis morbilli sociabantur, aliquibus petechiæ."

(*Hist. Anat. et Med. Rar.*, cent. v, hist. vi.)

Four years later, in 1661, there occurred in England the famous fever "chiefly infestous to the brain and nervous stock," described by Willis, identified by him with the German Kriebelkrankheit of 1595-96-97, and recognized by Saillant, in 1776, in a wonderfully lucid paper, as the convulsive epidemic malady wrongly attributed by some to ergotism, and confounded with the gangrenous ergotism of Sologne.

Saillant, in this paper, which has somehow escaped the German bibliographers, in accordance with their wont, makes it clear that, though called by him the *Morbus Convulsivus Epidemicus*, this malady was as protean as only epidemic encephalomyelitis (or influenza) can be, and that in different years, and in different places, different clinical types occurred.

The famous "feavour" of Willis, and the "comatose fever" described by Sydenham, were shown by Dr. Charles Creighton, thirty years ago, to stand for a definite form of illness that, when Dr. Creighton wrote, was not recognized by nosographers.

The riddle is now resolved. Willis's fever represented a convulsive, and Sydenham's a lethargic form of encephalomyelitis occurring epidemically. The details of the argument were given by me in the Chadwick Lectures (1918), as yet unpublished, but it may here be said that Willis's fever was exactly reproduced in Queensland during 1917 (*cf.* Breinl), where even the flexor spasms, so long and so erroneously held to be characteristic of "ergotism," were observed, as was sometimes the case in London, during 1918, amongst our cases of "encephalitis lethargica."

The European influenzas of 1674-75 were preceded or accompanied by "epidemic psychoses" in Sweden (1673), the Kriebelkrankheit again in Germany (1672-75), malignant fevers with spasms in France (1673), and the comatose fever of Sydenham (Willis's fever of 1661), in 1673-74-75.



Henceforward, until 1800, the history of epidemic encephalomyelitis is that of Kriebelkrankheit (or Raphania, as it came to be called) in Germany, Scandinavia and Russia, of nervous fevers in Britain, of epidemic apoplexies and paralyses in Italy, and of nervous, comatose, lethargic, apoplectic, paralytic, spasmodic and convulsive fevers, as well as of spontaneous "hydrophobias," described by Werlhof, Saalman, de Sauvages, Selle, Vogel, Andry, Hillary, Wintringham, Gilchrist, Grant, and many other epidemiologists and systematists. Much material has been collected: much more perhaps remains for investigation. But one or two landmarks may be pointed out. For example: Albrecht of Hildesheim had, in 1695, described a typical case of encephalitis lethargica in these words (*Miscell. Curios.*, an. ix and x, obs. i):—

"DE FEBRE LETHARGICA IN STRABISMUM UTRIUSQUE OCULI DESINENTE."

"Ahno 1695, virgo hujus loci, viginti circiter annorum, honesti cujus tam civis I.F. filia, in febrem incidit continuam, acutissima cephalalgia siccitate oris et aliis, quæ in ejusmodi morbis acutis notari sunt, symptomatibus stipatam, quorum tamen præcipuum circa, hoc subjectum in summa ad somnum propensione consistebat, quæ quo magis capitis remittebat dolor, majus majusque capiebat incrementum, ita, ut quoties a somno excitaretur toties in eundem relaberetur profundissimum.

"Scilicet, a quo tempora meliori prædita erat valetudine, oculorum talis advertebatur distortio, quæ pupillam in utroque versus palpebram adigebat superiorem, inferiori bulbi parte ultra ejus dimidium non nisi album referente."

Later, the famous influenza of 1712, notoriously cephalic and nervous, was signalized at Tübingen by the epidemic, of which so much has been said lately, usually referred to as the "Schlafkrankheit." It is not generally stated that R. J. Kammermeister, who described it, called it an epidemic febrile catarrh, and identified it with the pandemic of 1580, of which I have spoken. I cite some salient passages:—

"Hæc autem pleraque omnia quadrabant iterum in febrem catarrhalem hujus anni 1712. Fuit hæc universalis, popularis maxima gravis capiti, sub concursu forte trium, febris, catarrhi, vomitus, magis afflicto; sive contagiosæ vel epidemiæ predicatum meruisse dicenda sit. . . . Gravedo ista quondam Germanis die 'Schlafkrankheit' dicta fuit, nunc agrypnia, nunc veterno molestior. Hæc vice nomen illud non audii. Nec dormivisse multum nemini, præterquam paucos, opiatis quidem non usos. Noctes utique graves, turbatæ phantasiis



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frequens etiam per diem querela de afflictis oculis, utut non inflammatis, ægre tamen aperiendis, nec lucem ferentibus. . . . Eadem Gallis olim audiit 'Coqueluche.'"

(*Ephemerides*, cent. iii and iv, t. xxvii, obs. lviii.)

It is on this account that von Economo relies, when suggesting that encephalitis lethargica was recognized, as a "clinical entity," by Camerarius and by precedent observers. Whatever we may think as to the identity of the cases seen by Camerarius with those seen at Vienna during 1917 (and Professor Netter is inclined to be critical, though accepting Albrecht's case), there can be no doubt that influenza prevailed at Tübingen during 1712, and was accompanied by encephalitic manifestations.

I have, however, failed to find any evidence that the name "Schlafkrankheit" had previously obtained currency, and am inclined to believe, as already stated, that there had been a perversion, not without significance, from the earlier nicknames of "Schaffkrankheit" and "Schaffhusten." There may even have been a printer's error!

Much more important, however, than Camerarius's short essay is the account given by Guidetti (in Bianchi's *Historia Hepatica*, 1725, p. 718) of the epidemic constitution for 1712 as observed at Turin. The parallel with that of 1918 at London is extraordinary, and, clearly, "epidemic stupor" is no "new disease."

Some passages may be given from Guidetti:—

"Ad Januari principium nebulae adhuc contumaces in tenuem pluviam liquescebant et statim inter morbos catarrhales varios puta tusses raucedines et ptyalismos irrepsero febres frequenter soporosa, provectis aequae ac juvenibus infensae cum frigido ad caput decubitur, quem febris quidam imminuta prosequabatur. Aegri interim lente moriebantur vel comatosi vel cataleptici vel aphoni. Plurimi ante obitum convulsionibus torquebantur."

It is moreover interesting to note that Heusinger, in his *Commentatio Semiologica*, actually connoted Guidetti's account with that of Willis, and that, according to Guidetti, the "rheumatic epidemic," for so he termed the influenza of 1712, spread, in the late autumn, "inequaliter sed celeriter, per totam Italiam."

The still more famous influenza of 1729-33 was, singularly enough, marked at Tübingen in 1729 by an undoubted encephalomyelitis of convulsive type. Elias Camerarius, who described it (*Act. Phys. Med.*, ii, obs. cli) clearly recognized the essential unity of the nervous

disease and the catarrhal cases. This seems rather to have baffled the writers on ergotism, for they have left the account of Camerarius on one side. The common people, as always, he said, accused the weather, the grains, the bread, and the unripe fruits. But he himself thought these but vague conjectures, and expressed no opinion of his own.

In the latter part of 1727, however, Scheffelius had published what is now a somewhat rare essay, entitled, "*De Morbo Epidemio Convulsivo, per Holsatiam grassante oppido raro.*" The malady, evidently the same as that which occurred at Tübingen in 1729, had been observed by Scheffelius in the spring and summer of 1727. Identified by not a few as the old Kriebelkrankheit, it was claimed by others as certainly due to ergotism, though Scheffelius declared many to have been affected who had not eaten questionable bread. The nature of Scheffelius's powerful argument may be inferred from some of his rubrics:—

"An morbus novus sit?"

"Epidemici paucissimi sunt novi: exemplo febris catarrhalis 1712."

"Et morbi nostri convulsivi, teste Willisio et aliis, Horstius eundem morbum descripsit."

"Natura ipsa non est causa."

"Morbum hunc a panis vitio apud nos productum esse non est verosimile sed ex aeris peculiari quadam constitutione."

"Verum istud contagium non est absolutum."

The identification with Willis's fever is remarkable enough, but it is even more noteworthy that Scheffelius found traces of the "same disease" as this of 1727, in some particular accounts of the influenza of 1580, and his insight was vindicated by the recurrent waves of influenza that continued from 1729 to 1733 throughout the world.

A few years later Kriebelkrankheit, both convulsive and paralytic, was in Brandenburg (1741) the forerunner of influenza in Germany (1742), and the pandemic of 1743; while, in 1745, the same or a similar meningeal, encephalitic and myelitic malady trailed through Sweden, giving rise again to vague conjectures, but being, on the whole, identified clinically with its German congener.

Sequential paralyses were noted: the acute cases were stuporose, mute, and had ocular disturbances.

1754-55-56 and 1757 saw a recurrence in Sweden, again with stupors, delirium, psychoses and mutism, but with convulsions rather than paralyses. This terminated, in 1758, in a peculiar kind of "influenza" (Ozanam).

Boström indeed, at Upsala, had, in 1757, triumphantly identified the endemic-epidemic of these years, known as the Upsala fever and marked by head-retraction, with a "long known protean fever, everywhere prevalent from time to time, sometimes in one form, sometimes in another." "*Hic morbus non est novus*," he declared. Nevertheless, the trailing epidemics in the rural districts had again been identified on clinical grounds with the Kriebelkrankheit, though shown clearly *not* to be due to ergot. This being so, Rothman, a pupil of Linné, and with that great man's approbation, elaborated the hypothesis that this stuporose, delirious, paralytic and convulsant "fever," possibly contagious, was caused by radish seeds in the threshed grain. It was therefore christened Raphania: and the disease was known as such for nearly a hundred years. Meanwhile the first case of botulism (or encephalitis due to sausage poisoning) is said, by Kerner, to have been described in Germany in 1755, while Raphania, as we must now call it, there occurred at the same time.

The influenzas of 1762 were catarrhal rather than nervous; but Raphania was again severe in Brandenburg and Zell in 1770, and was held by Selle, amongst other German physicians, to be feebly contagious, a fever, and different, by all the heavens, from true ergotism; while 1771 saw a genuine and severe influenza in Hesse, and 1772 influenza and epidemic convulsions in North America. About this time Leidenfrost and Schlegel protested vigorously against the notion, again gaining ground, that the acute paralytic, spasmodic malady had something to do with the gangrenous, and the chronic forms of ergotism, but in vain; though Haberkorn, earlier, had properly defined it as "*die Nervenkrankheit*."

However, 1773 was the year of Sir Walter Scott's infantile paralysis and, in 1772-73-74, the so-called miliary fever prevailed extensively in France, accompanied by nervous manifestations such as coma and convulsions (Baraillon). In 1775 Andry described admirably what must have been acute bulbar encephalitis in a young woman—he called it "hydrophobia without the bite of a dog"—and, in London, Grant declared that, during the influenza of that year he had lost several patients with the "Comatose Fever" of Sydenham.

During the influenza years 1780-81-82, Butter, under the name of "infantile remittent fever," observed what was clearly the acute stage of encephalomyelitis, describing it as a complaint both epidemic and sporadic, and affecting adults as well as children, while, two years later (1784) Michael Underwood first noted, as "debility of the lower

extremities," the deformities resulting from what must have been the same acute illness.

A celebrated institutional outbreak in Turin, in 1789, has been handed down by copyists as *Raphania*; but the accounts given by Corradi indicate, I think, clearly either an encephalitis or a cerebro-spinal meningitis; moreover influenza was raging in the city at the time.

The third chapter of my story may perhaps be taken to commence in 1800, when Chardel, of Paris, described cerebral fever, or primary inflammation of the brain, as a definite entity: 1799 and 1800 was an influenza season. The world-wide influenza prevalences of 1800-03 were noted as extraordinarily "cerebral" in Russia; and *Raphania* was recorded there (as again in Scandinavia) in 1804.

The Italian influenza of these years was also very "cerebral," and it was his then experiences, apparently which led Zeviani to consider the old "*mal mazzuco*" as "influenzal," or at least derived from the "epidemic catarrh." The celebrated "cerebro-spinal meningitis" at Geneva was in 1805; that of Massachusetts in 1806.

A very interesting point now arises. Influenza prevailed extensively in Hindostan about 1800-03, and John Shaw, of London, writing of deformities in 1823, described the case of a young man whose disability dated from an attack of paralysis, evidently poliomyelitic, that he suffered during his infancy in India. Shaw went on to say that he had been told that such "sudden attacks" were common among children in India.

Dr. Ager, of Brooklyn, in a recent paper, lays it down, on the strength of this suggestive remark, that infantile paralysis prevailed to some extent amongst Anglo-Indian children in 1800, and hints that it is really an Asian malady. The coincident appearance of epidemic influenza in India, about the year 1800, does not appear to have struck him as noteworthy. Feiler, however, writing from Salzburg in 1814, described a case of "shank-shrinking," as he called it, in a girl aged 12 or 13, afflicted since infancy. She too must have suffered about 1802, the year of the so-called sweating-sickness at Röttingen, which was identified, in the midst of influenza, as the mediaeval sweating sickness come back again (Hecker).

Influenza in Europe occurred only in the endemic-epidemic form, though severely, between 1819 and 1824; and many outbreaks were in France and Germany described as miliary fever, or "sweating-sicknesses." It was during these years that Kerner, in Würtemberg,

first described the "Sausage Disease," afterwards known as botulism, and that Abercrombie in Britain and Hutin and others in France and Germany, gave so much attention to encephalitis.

Epidemic influenza was severe in the United States in 1824-25-26; indeed, in 1824 Raphania was diagnosed clinically in a certain prison in New England, while, in 1826, Jones declared he had noted the severity of "phrenitis" as well as other nervous affections in the "late influenzas."

The influenzas, in Europe, of 1831, 1833, and 1836-37, gave rise to a perfect exuberance of literature concerning encephalitis and myelitis in France, while, in Germany, we hear again of Raphania, by now being examined critically.

In Würtemberg, botulism and acute encephalitis were described within a few miles of each other, in 1834 and 1835. In the same years and in the same kingdom Heine noted his first cases of infantile paralysis, while 1835 saw Badham's cases of the same malady in England, and the publication of lectures by Ryan, a long forgotten London physician, describing, *inter alia*, cerebral, bulbar, and spinal forms of encephalomyelitis in children.

The medical history of these years is indeed remarkable. Lombard, writing from Geneva to the *Gazette Médicale de Paris* (1831 and 1837) drew attention to an unpublished paper by Peschier (1820) describing the cerebral and nervous forms of the influenzas of that period when Kerner was then ascribing to "sausage poisoning" certain like "clinical entities" that Stoker, afterwards, declared he had seen, in the same year, at Dublin. But Lombard expressed an aphorism that is worth recording, since it embodies the experience of Hippocrates, of Ballonius, of Bartholin, of the two Kammermeisters, and of Guidetti.

He said: "*La grippe est souvent précédée par une constitution éminemment nerveuse, dont les caractères principes sont de porter le trouble dans les fonctions du cerveau et des nerfs encéphaliques.*" Ducros, Montain, Pétrequin and Récamier made clinical observations in the same sense, and Gintrac, of Bordeaux, in a paper that I have not seen, described "epidemic stupor in children"—"coma sans danger"—as prevailing in the early spring of that notable influenza year, 1837. Malcorps, of Brussels, went further. He divided the historic influenzas into two categories: one, vernal, catarrhal, and benign, as in 1658, 1742, 1743, 1762, and 1780; the other, autumnal, or hiemal, and marked by "prodromes nerveux, caractère adynamique, gravité plus grande," as in 1580, 1676, 1730, 1737, 1775, and 1837.

Surely our "encephalitis lethargica" of 1918 should be reckoned amongst the "prodromes nerveux" of the influenza of 1918, which, in point of fact, combined Malcorps's two categories.

The influenzas of 1841-45 were evidently accompanied by much infantile paralysis in the British Isles, described by West, Kennedy, and MacCormac: much encephalitis, cerebro-spinal meningitis and "cerebral typhus" in France; encephalitis, botulism and more infantile paralysis in Germany; and, in Italy, the extraordinary "Tifo apoplettico-paralytico-tetanico," which, though now thought to have been cerebro-spinal meningitis, was, at the time, identified clinically (1) as the sweating sickness of the Middle Ages (Agostinacchio), (2) Raphania (Semmola), and (3) encephalitis and influenza.

In Scandinavia and Russia, Raphania and epidemic psychoses prevailed throughout these years, while the influenzas in the United States during 1842-43 had been preceded by the outbreak of infantile paralysis described by Colmer in 1841, and Dunglison had noted the great increase of encephalitis everywhere at home and abroad.

The great influenza pandemic of 1847 was mainly catarrhal, but the lesser waves of 1850-51, 1855, and 1857 were very "nervous."

In Württemberg, in 1850-51, there were again outbreaks of botulism and encephalitis; and the famous epidemic of Calw, in Fritz's essay glorified as one of the spinal and bulbar forms of typhoid, was either Heine-Medin disease or nothing.

Raphania was flickering out in Sweden in the "fifties," for it then and there was beginning to be called cerebro-spinal meningitis, but, at the same time south-western Germany and Bavaria, with Hesse-Nassau, again suffered an extraordinary medley of outbreaks of botulism, Raphania, localized influenzas, encephalitis and the like diagnostic "entities." In 1856 Heusinger, of Marburg, studied the question of acute and chronic ergotism in the light of actual experience and came to the conclusion that some of the old epidemics had been probably typhus—i.e., "cerebral typhus," or cerebro-spinal meningitis and encephalitis.

But this medley dissipated until influenza came back, not as a great pandemic, but diffusedly, in 1866-67. There had been some infantile paralysis at Paris just before: but botulism and Raphania again appeared in Württemberg and adjacent districts in these years, during which Stuttgart suffered severely from influenza.

The last trace of Raphania and epidemic psychopathy in Sweden (1868) coincided with the first recognized outbreak of poliomyelitis in Norway (Ruhräh).



Poliomyelitis was epidemic on quite a large scale in Philadelphia in 1871-72-73-74; influenza was "universal" in the States in 1873, and continued diffused therein until 1875, reaching France in 1874-75; and the first recorded epidemic of poliomyelitis in that country was in 1875.

1880-81 is a year now generally recognized as one of scattered influenzal prevalences—it was then that Wernicke and Etter first described cases of "polio-encephalitis acuta hæmorrhagica."

Poliomyelitis was then epidemic in Sweden and noticeable in England also, while in 1884 Strümpell enunciated his now well known views on the essential identity of polio-encephalitis and poliomyelitis.

The pandemic influenza of 1889-90 was immediately preceded by the Swedish outbreaks of "infantile paralysis" studied by Medin, and by the scattered diffusion in the Mediterranean basin of a "new disease," afterwards decided to be cerebro-spinal meningitis (Bezly Thorne). It was followed by the famous "Nona" of Lombardy and Hungary, identified by Netter with the "encephalitis lethargica" of last year and this—the newest of new diseases! Yet surely it was none other than the old mal mazzuco!

We reaped an aftermath of the great 1889-90 pandemic in minor waves of influenza, accompanied by encephalitis throughout the world, till 1895. In 1895 there was not only the Stockholm poliomyelitis, but, very curiously, an epidemic of "grippe" and acute encephalomyelitis at Toulouse, studied by André, who described it in his book on influenza, declaring that polio-encephalitis had proved to be a contagious malady, and suggesting that it represents a local and intense form of "grippe nerveuse."

About this time, too, Oppenheim and Cassirer had rediscovered Wernicke's "encephalitis acuta hæmorrhagica" and had shown it to be, in the main, influenzal.

Moreover, it was also in 1895 that van Ermengem observed the Belgian outbreak which, while clinically polio-encephalitis, was declared to be the old Swabian "botulism," and ascribed to an organism which has not been found more than once, if ever, in the body of anyone dying of this alleged "disease." It is true that this bacterial botulism of van Ermengem cannot be distinguished *clinically* from the older sausage disease of Justin Kerner, but it is also clinically identical with the stuporose forms of the mal mazzuco and Raphania.

The convulsive forms of the mal mazzuco and of Raphania, on



the other hand, are indistinguishable clinically from the convulsive, or spasmodic forms of Heine-Medin disease described by German and Austrian observers a few years ago, and from the "mysterious disease" epidemic in Australia during the spring of 1917.

The events of the last twenty-five or thirty years have, however, not yet attained the dignity of history. Still, without doubt, culminating as they do in the recent world-cycle of poliomyelitis, polio-encephalitis, cerebro-spinal meningitis and influenza, they amply vindicate the view as to the epidemiological relation at least between these diseases, expressed, for poliomyelitis by Brorström in 1910 and for cerebro-spinal meningitis by Dr. Hamer, on many occasions.

In this connexion reference should be made to the important paper by Looft, which may be found in the *Nord. Medic. Arkiv* for 1901, (afd. ii, Häft i). Looft, while professedly giving the history of cerebro-spinal meningitis in Norway between 1875 and 1897, throws into high relief the extraordinary clinical and epidemiological relationship between polio-encephalitis, poliomyelitis, cerebro-spinal meningitis, and epidemic catarrh. For, without doubt, many of the cases ascribed by him to the third of these diseases, and shown to be connected with the fourth, would, more justly, have been attributed to either the first or the second: a point that has been suggested also by Foster and Gaskell.

But the relationship between these "diseases," and some others as well, is, to those who have examined the evidence, not superficial and based upon any confusion. The confusion has arisen by reason of well-meaning attempts to establish an artificial, even if convenient, set of distinctions as something which corresponds to realities in nature.

Independent observers, such as Lewis in America (*Interstate Medical Journal*, 1918, v, p. 396) and Saunders of Grahamstown, are everywhere now contributing their quota, and formulating their conclusions, in support of the synthetic tendency. The recent experiences of Marcus at Stockholm (*Berliner klinische Wochenschrift*, 1918, lv, pp. 1151-2) and the observations of Sainton, and of Chartier (*Presse Médicale*, 1918) should not pass unrecorded.

In the recent Chadwick lectures I dealt at greater length than is now possible with the history of all these affections: and I then tried to show, as to-day, that their epidemiological association (if we have regard to realities and not to names, or to concepts) has been repeatedly recognized since the time of Hippocrates.

This association, recognized by Boström in 1757 and by Zeviani in 1804, will undoubtedly be again discovered in the near future.

In the meantime the position may perhaps be thus summarized :—

(1) Clinical occurrences of the nature that we now ascribe to encephalomyelitis, or encephalo-myelo-meningitis, have been recorded in modern times for at least 450 years.

(2) In great part these occurrences have been noted as incidental to major prevalences, known historically as the sweating sicknesses, the influenzas, or epidemic catarrhs, and the like.

(3) But special epidemics of these occurrences have also been described as manifestations of special diseases. These special epidemics have usually appeared shortly before or shortly after major "influenzal" prevalences, or else in geographical proximity to endemic-epidemic and endemic influenzal prevalences.

(4) Epidemic encephalo-myelo-meningitis may represent an extensive specialized reaction that has perhaps the same epidemiological relation to pandemic influenza as have the prevalences and epidemics of "septic" pneumonia and of gastro-intestinal illness, described before and after that affection.

(5) In any case, owing to the relative infrequency of the *prevalences*, and their marked variation in type, historical investigation is necessary in order that contemporary occurrences be viewed in a correct perspective.

One detail deserves mention, here and now, for it shows the difficulty of historical investigation at short range. The great epidemic of poliomyelitis in and about New York during 1916 followed closely upon a prevalence of "grip" in the States, the like of which had not been known since 1889-90. Yet this wave which "swept through" a continent has completely eluded the attention of those who have written the "history" of our recent influenza! It was, however, well described by Capps and Moody, as well as by others, in the *Journal of the American Medical Association* for 1916.

Once more, there is nothing new in these notions. Many writers, but perhaps most notably Dr. Hamer in our time, have recognized the clinical affinities and epidemiological liaison between what we now call forms of epidemic encephalomyelitis and meningitis, on the one hand, and the epidemic catarrhal fever, or influenza, on the other.

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